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10/719,532	11/21/2003	David Follansbee	DAVFOL.002C1	3410

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EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	PAPER NUMBER
1644	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/719,532	FOLLANSBEE, DAVID	
	Examiner	Art Unit	
	NORA M. ROONEY	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 7-24* is/are pending in the application.

4a) Of the above claim(s) *7,9,10 and 13-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 8 and 11-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/28/2008 has been entered.

2. Claims 7, 9-10 and 13-24 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 09/19/2006.

3. Claims 1-2, 8 and 11-12 are currently under examination as they read on a pharmaceutical formulation for increasing blood serum levels of Immunoglobulin E levels (IgE) in a mammal comprising at least one helminth-based antigen.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-2, 8 and 11-12 *are* rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: a composition comprising homogenized and filtered *Capillaria hepatica* and *Dicrocoelium dendriticum* worms and/or antigenic material isolated by

placing Capillaria hepatica and *Dicrocoelium dendriticum* in saline solution to extract antigens; does not provide reasonable enablement for: **a pharmaceutical formulation for increasing blood serum levels of Immunoglobulin E levels (IgE) in a mammal** comprising: at least one **helminth-based antigen**, wherein said **helminth-based antigen** comprises **a protein of at least approximately 50,000 molecular weight obtained from a helminth selected from the group consisting of *Capillaria hepatica* and *Dicrocoelium dendriticum*,** wherein said **helminth-based antigen increases said mammal's blood serum levels of Immunoglobulin E levels (IgE) to greater than about 3,000 IU/ml thereby ameliorating the allergic reaction of said mammal to a plurality of antigens** of claims 1-11; and **an extract for treating allergies or asthma in a mammal** comprising the **pharmaceutical formulation of Claim 1 in an amount sufficient to regulate IgE** of claim 12.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the

amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

On pages 25-28, the specification discloses a composition comprising homogenized and filtered *Capillaria hepatica* and *Dicrocoelium dendriticum* worms and/or antigenic material isolated by placing *Capillaria hepatica* and *Dicrocoelium dendriticum* in saline solution to extract antigens.

As stated previously in the Office Actions mailed on 03/19/2007 and 08/14/2007, although the benefit of some helminths to downregulate allergic responses has been documented, Carvalho et al. (PTO-892 mailed 03/19/2007, Page 2, Reference V) teaches that helminths synthesize protease molecules that provoke allergenic responses and that excretory/secretory products of helminths can actually induce Th2 responses. In addition, some helminthic antigens cross-react with allergens which can increase allergic reaction in atopic individuals and initiate allergic diseases in non-atopic individuals (In particular, page 529, paragraph spanning left and right columns). Wilson et al. (PTO-892 mailed on 03/19/2007, Page 3, Reference U) teaches that helminth-driven suppression of allergic inflammation is mediated by CD25+ upregulated T cells. However, expression of CD25 depends on both many defined and as-yet unknown factors (In particular, abstract, page 1203, 'Anti-CD25 antibodies block supression' section). Expression is associated with the induction of specific cytokines, namely IL-10 and TGF- β, but there is no evidence in the reference or otherwise that all helminth antigens upregulate CD25 on T cells.

Cooper et al. (PTO-892 mailed 03/19/2007, Page 2, Reference W) teaches that geohelminthic parasites secrete potent allergens and can be capable of enhancing allergic inflammation as evidenced by asthmatic symptom decrease upon anti-helminthic treatments (In particular, page 399 second to last paragraph of left column). Falcone et al. (PTO-892 mailed 03/19/2007, Page 2, Reference X) provides insight into the state of the art in disclosing that, as of 2005, clinical trials were ongoing. If positive immunosuppressive results are demonstrated, those parasites will be then mined for immuno-suppressive molecules that can be used in appropriate sustained-delivery formulations to mimic successful immunological responses induced by natural infections. (In particular, page 159, paragraph spanning left and right columns).

Further, Lynch et al.(PTO-892; Reference U) teaches that the intensity of the polyclonal IgE response induced by helminthic infection impacts whether or not allergic disease is enhanced or suppressed and that the interaction is complex and based upon both the allergic disease and the helminthic infection (In particular, page 50, right column, page 53, right column, first paragraph). In addition, Erb et al. (PTO-892: Reference V) teaches that the mechanism whereby helminthic infection suppresses allergic disorders is, as of 2007, unknown. Therefore, the art of helminthic based pharmaceutical compositions for the treatment of allergies is highly unpredictable.

Given the state of the art discussed *supra*, one of ordinary skill in the art would be required to perform undue experimentation to determine which helminthic based antigens of at least 50,000 molecular weight obtained from *Capillaria hepatica* or *Dicrocoelium dendriticum*

would have the requisite functions of being able to increase a mammal's blood serum levels of IgE to levels greater than about 3,000 IU/ml, to ameliorate the allergic reaction to a plurality of antigens and to treat allergies or asthma in a mammal. In particular, the art teaches that total and helminthic antigen-specific IgE levels change over time in response to helminthic infections and that the intensity of the helminthic infection impacts whether or not allergic disease will be ameliorated or exacerbated. It is highly unpredictable, especially due to the lack of guidance in the specification, as to whether any particular antigen from *Capillaria hepatica* or *Dicrocoelium dendriticum* can be used *in vivo* to simulate the amelioration of allergic disease induced by helminthic infections. It is also unpredictable how such an antigen, if found, would be administered in vivo. Further, the amelioration of all allergic reactions to any antigen is encompassed by the instant claim recitation. However, the specification has provided no guidance on how to ameliorate any particular allergic reaction to any particular antigen, much less all allergic reactions to all antigens, as encompassed by the instant claim recitation.

The specification has not adequately disclosed a pharmaceutical composition that can be used to ameliorate the allergic reaction to "a plurality of antigens" as recited in claim 1. Antigens that induce allergic reactions, or allergens, are a diverse group of compounds which elicit diverse allergic responses. For example, food allergens and inhalation allergens induce different reactions and what is a treatment for one response will not necessarily be an effective treatment for another. Therefore, it would require one of ordinary skill in the art to perform an undue amount of experimentation to make and use a pharmaceutical composition comprising a helminth based antigen that will ameliorate the allergic reaction to any antigen.

The specification has not adequately disclosed "a protein of at least approximately 50,000 molecular weight" as this recitation has no indication of the units.

In addition, helminthic extracts obtained from *Capillaria hepatica* and/or *Dicrocoelium dendtriticum* comprising a helminthic based antigen of at least 50,000 molecular weight as the extract disclosed on pages 25-26 of the specification, will contain helminthic components that are not responsible for decreasing allergy and may actually cause separate, unpredictable inflammatory responses or other undesirable side-effects. Therefore, the specification has not adequately disclosed a pharmaceutical composition comprising proteins of at least 50,000 molecular weight obtained from *Capillaria hepatica* and/or *Dicrocoelium*.

Since no *in vivo* studies were used as model system to treat any allergic reaction, allergy or asthma, it is not clear that reliance on the *in vitro* data accurately reflects the relative animal efficacy of the claimed therapeutic strategy. The specification does not adequately teach how to effectively treat any allergic disorder or to reach any therapeutic endpoint in animals by administrating the pharmaceutical formulation comprising a helminthic based antigen of at least 50,000 molecular weight obtained from *Capillaria hepatica* and/or *Dicrocoelium dendtriticum*. The specification does not teach how to extrapolate data obtained from the *in vitro* studies to the development of an effective *in vivo* therapeutic treatment, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the substance that ameliorates allergic reactions, increases IgE to greater than about 3,000 IU/ml

and treats allergies or asthma, as encompassed by the claimed invention. There must be a rigorous correlation of biological activity and an *in vivo* effectiveness to establish a method of treatment of such allergic disorders. The specification does not provide sufficient teaching as to how it can be assessed that treatment of such allergic disorders is achieved after the administration of the pharmaceutical formulation of the invention.

Substantiating evidence may be in the form of animal tests, which constitute recognized screening procedures with clear relevance to efficacy in humans. See Ex parte Krepelka, 231 USPQ 746 (Board of Patent Appeals and Interferences 1986) and cases cited therein. Ex parte Maas, 9 USPQ2d 1746.

Although, the specification describes *in vitro* experiments, there is no correlation on this record between the in vitro studies and the various methods of treating allergic disorders in mammals. It is not enough to rely on in vitro studies where, as here, a person having ordinary skill in the art has no basis for perceiving those studies as constituting recognized screening procedures with clear relevance to efficacy in humans or animals (emphasis added). Ex parte Maas, 9 USPQ2d 1746.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Applicant's argument filed on 05/28/2008 has been fully considered, but is not found persuasive.

Applicant argues:

> "Applicant has amended Claim 1. The Office states that there is "no data to enable the claims." Applicant believes that the Examiner's request for data was based on the breadth of the previously presented claims. In view of the amendments identified above, Applicant asserts that the specification provides ample support for the claims. However, any subsequent argument by the Examiner that data is required to support the amended claims would, respectfully, be unfounded. It is well-established that an applicant is not required to submit data to establish enablement. For example, in *Ex Parte Kyle,* the Board of Patent Appeals and Interferences reversed the Examiner's rejection of claims and explained:
>
> > The examiner has not explained why the specification's straightforward protocols for synthesizing, identifying and using bradykinin antagonists, together with what was known in the art at the time of the invention, does not satisfy the enablement requirement of 35 U.S.C. § 112.
> >
> > Finally, to the extent that the examiner requires an assurance of certainty ("[t]here is insufficient bioassay data provided ... which teaches that all of the possible Bk analogs would be effective as antagonist," (Examiner's Answer, page 3)) to demonstrate enablement, we note that no legal authority has been cited in support of this requirement. On the contrary, a requirement for certainty would be incompatible with any experimentation at all. Accordingly, the rejection of claims 1, 2, 4 and 5under 35 U.S.C. § 112, first paragraph is reversed.
>
> *Ex Parte Kyle,* 2000 WL 35451360, *4 (Bd.Pat.App. & Interf.). *See also Carter-Wallace, Inc. v. Riverton Laboratories, Inc.,* 433 F.2d 1034, 1037-1038 (2d Cir. 1970) (emphasizing that "submission of test information to the Patent Office in support of the claims made in an application is not required, unless the asserted utility of a compound is not believable on its face to persons skilled in the art in view of the contemporary knowledge in the art."). Here, the asserted utility of the claims should not be questioned. Indeed, the Examiner has not rejected any of the claims under § 101 for lack of utility. Moreover, in light of the Examiner's reliance upon prior art that allegedly anticipates or obviates Applicant's claimed invention, it would be inconsistent for the Examiner to later allege that the asserted utility of a helminthic antigen for treating allergies or asthma is not believable to persons skilled in the art. In view of the above amendments and remarks, the Applicant respectfully requests that the Examiner withdraw the written description and enablement rejections."

It is the Examiner's position as set forth *supra* that the art is unpredictable and as such would require one of ordinary skill in the art to perform undue experimentation to practice the invention commensurate in scope with the claims. The factors most relevant to this enablement rejection are the scope of the claim, the amount of direction or guidance provided, the lack of

sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. Without sufficient working examples and guidance in the specification on how to make and/or use the recited pharmaceutical formulation, the claims are not enabled. Contrary to the facts in Ex Parte Kyle, the instant Examiner has set forth in detail *supra* why the claims are not enabled. The instant rejection is not a utility rejection, so Applicant's arguments with regard to utility are not germane. Therefore, the rejection stands.

6. Claims 1-2, 8 and 11-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of: a composition comprising homogenized and filtered *Capillaria hepatica* and *Dicrocoelium dendriticum* worms and/or antigenic material isolated by placing *Capillaria hepatica* and *Dicrocoelium dendriticum* in saline solution to extract antigens.

Applicant is not in possession of: a pharmaceutical formulation for increasing blood serum levels of Immunoglobulin E levels (IgE) in a mammal comprising: at least one **helminth-based antigen**, wherein said **helminth-based antigen** comprises **a protein of at least approximately 50,000 molecular weight** obtained from a helminth selected from the group

consisting of *Capillaria hepatica* and *Dicrocoelium dendriticum,* wherein said **helminth-based antigen increases** said mammal's blood serum levels of Immunoglobulin E levels (IgE) to greater than about 3,000 IU/ml thereby ameliorating the allergic reaction of said mammal to a plurality of antigens of claim 1; and **an extract** for treating allergies or asthma in a mammal comprising the pharmaceutical formulation of Claim 1 in an amount sufficient to regulate IgE.

Applicant has disclosed only a composition comprising homogenized and filtered *Capillaria hepatica* and *Dicrocoelium dendriticum* worms and/or antigenic material isolated by placing *Capillaria hepatica* and *Dicrocoelium dendriticum* in saline solution to extract antigens; therefore, the skilled artisan cannot envision all the contemplated pharmaceutical composition possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method.

Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant

was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-2, 8 and 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Bode et al. (PTO-892; Reference W).

Bode et al. teaches a composition comprising *Dicrocoelium dendriticum* fluke extract in distilled water (In particular, page 169 'Antigens' section, whole document). The reference distilled water is both a pharmaceutically acceptable diluent and carrier. The crude fluke extract is in liquid form and, as such, is also an injectable fluid.

The recitation of "a pharmaceutical composition for increasing blood serum levels of Immunoglobulin E in a mammal" in claim 1; and "for treating allergies or asthma in a mammal comprising the pharmaceutical formulation of Claim 1 in an amount sufficient to regulate IgE" in claim 12 is inherent because the reference crude fluke extract is compatible with the non-limiting definition of a pharmaceutical formulation in the specification. The claims read on the active or essential ingredients of the composition. Therefore, the reference crude fluke extract is encompassed. Further, giving the terms their broadest reasonable definition, crude fluke extract in distilled water is not incompatible with pharmaceutical use for treating allergies or asthma in a mammal.

The reference *Dicrocoelium dendriticum* fluke extract inherently comprises a protein of at least approximately 50,000 molecular weight that increases said mammal's blood serum levels of Immunoglobulin E levels (IgE) to greater than about 3,000 IU/ml thereby ameliorating the allergic reaction of said mammal to a plurality of antigens" of claim 1 because the whole fluke

extract necessarily comprises all antigens of *Dicrocoelium dendriticum*, including the recited antigen or antigens.

Claim 8, which recites "wherein said protein is recombinant," is included in this rejection because the patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985) See MPEP 2113. Once a product is fully disclosed in the art, future claims to that same product are precluded, even if that product is claimed as made by a new process.

The reference teachings anticipate the claimed invention.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

March 2, 2009

Nora M. Rooney

Patent Examiner

Technology Center 1600

/Nora M Rooney/

Examiner, Art Unit 1644